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Full Length Article

Hypofractionated Volumetric Modulated Arc Radiotherapy with simultaneous Elective Nodal Irradiation is feasible in prostate cancer patients: A single institution experience

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KEYWORDS

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Abstract *Purpose:* To assess feasibility, toxicity and biochemical relapse-free survival (b-RFS) for a group of organ confined (OC) Saudi prostate cancer patients treated by hypo-fractionated Volumetric Modulated Arc Radiation Therapy (VMAT) Simultaneous Integrated Boost (SIB) Elective Nodal Irradiation (ENI) whole pelvic radiotherapy (WPRT).

Patients and methods: Between March 2009 and January 2014, 29 OC prostate cancer patients; median age 64 years, PS 0–1 were treated in King Faisal Specialist Hospital – Riyadh, Kingdom of Saudi Arabia using VMAT–SIB–ENI–WPRT, to a total dose of 70 Gy in 28 fractions. Twenty Four patients (83%) were treated with neo-adjuvant; concurrent androgen deprivation therapy (ADT). Median follow-up (FU) was 42 months (range: 18–72 months).

Results: The 3-year actuarial b-RFS for low/intermediate and high risk groups were 100%, and 48%, respectively ($p = 0.09$) with a median FU period of 34 months (range: 14–53 months). Gleason Score ($p = 0.02$), and pretreatment PSA ($p = 0.01$) were predictive for biochemical failure on univariate analysis; with no observed prostate cancer-related deaths. Grade 2 acute/late GI and GU toxicities were 28%/0% and 17%/10% respectively with no reported grade 3/4 toxicities. Four

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(50%) out of the 8 patients with baseline partial potency, retained sexual function on long term follow-up.

Conclusions: Hypo-fractionation dose escalation VMAT–SIB–ENI–WPRT using 2 arcs is a feasible technique for intermediate/high risk OC prostate cancer patients, with acceptable rates of acute/late toxicities, much favorable planning target volume (PTV) coverage, and shorter overall treatment time. Prospective randomized controlled trials are encouraged to confirm its equivalence to other fractionation schemes.

Introduction

Prostate cancer is the second most common solid tumor diagnosed in men in the United States and Western Europe [1]; a situation which is different in the middle east with reported incidence ranging from 4.7% to 6.4% of all cancers [2–3].

Treatment of localized prostate cancer has been proven by clinical trials including hypofractionation radiation therapy (RT) dose escalation with Elective Nodal Irradiation (ENI) [4,5] and androgen deprivation therapy (ADT) combined with RT [6,7]. Radiation therapy related toxicities is attributed to high total RT doses, short recovery time, and the volume of neighboring organs at risk [OARs] normal tissues (rectum and bladder) even in prostate-only RT [4–6]. Volumetric-modulated arc therapy (VMAT); a relatively new rotational radiation therapy intensity modulated radiotherapy (IMRT) technique delivering RT using continuous dynamic modulation of the dose rate, field aperture, and gantry speed in the treatment of whole pelvis (WPRT) or prostate only (±seminal vesicles) has been reported to be equal or better for target volume coverage and normal tissue sparing than IMRT [8]. One additional strategy to optimize the therapeutic ratio is hypofractionation, with the advantage of the assumption that prostate cancer is more sensitive than normal surrounding tissues to fractionation (low α/β ratio) [9]. Data from 7 databases (~6000 patients) evaluating prostate cancer clinical outcomes in relation to radiobiology confirmed the relatively low α/β ratio for prostate cancer control (range: 0.9–2.2 Gy); a ratio which is lower than the corresponding α/β ratios for late-responding tissues (3–5 Gy), with hypo-fractionation benefiting all risk groups with or without pelvic node irradiation [10]. Confirmatory meta-analysis supported prostate cancer low α/β ratio of $\leqslant$4 Gy [11]. Hypofractionation RT to the prostate only is now an accepted therapeutic alternative for high risk (HR) group of patients, with a weak evidence supporting concomitant pelvic node irradiation (retrospective phase I–II trials). Careful use of modern RT technologies with hypofractionation is a challenge to allow treatment of smaller volumes of critical structures (bowel, rectum, and bladder) [12].

To our knowledge; this study is the first experience in the Middle East Region using hypofractionated VMAT–SIB–ENI–WPRT technique with daily Image guided radiotherapy (IGRT) for a group of OC prostate cancer Saudi patients to assess its feasibility, toxicity and long-term b-RFS and to compare these outcomes with internationally published data.

Patients and methods

Between March 2009 and January 2014, 29 newly diagnosed, non-metastatic, biopsy-proven adenocarcinoma localized prostate cancer patients with no prior therapy; referred to radiation Oncology service – King Faisal Specialist Hospital (KFSH) – Riyadh, Kingdom of Saudi Arabia-KSA were treated with definitive Volumetric Modulated–Simultaneous Integrated Boost–Elective Nodal Irradiation–Whole Pelvis Radiotherapy (VMAT–SIB–ENI–WPRT) to a total dose of 70 Gy in 28 fractions (250 cGy/Fx). Patients with distant metastases or recurrent disease and those who did not complete their treatment, in addition to those treated with palliative intent were excluded from the study.

All Patients underwent pre-treatment trans-rectal ultrasound prostate biopsy; median number of cores collected was 9 [6–12]. Pre-treatment work-up included: MRI pelvis to evaluate extraprostatic extension, pelvic lymph node metastases and prostate volumetric assessment, CT scan of the chest–abdomen and pelvis and nuclear medicine (NM) bone scan. Patients were stratified to risk groups based upon current NCCN prognostic risk groupings (www.nccn.org). Baseline demographics and clinical characteristics of the treated group are shown in Table 1. Due to the small numbers of low risk (5 patients) and intermediate risk patients (4 patients), both groups were merged together as one group for statistical analysis.

Among the 29 patients; 24 (83%) were treated by androgen deprivation therapy (ADT): a total of 6-months for intermediate-risk patients (14%) and 2–4 months prior to VMAT–SIB–WPRT. While for high-risk patients (69%) ADT was continued to a total duration of $\geqslant$24–36 months. Biochemical failure was defined as per the Phoenix-Radiation Therapy Oncology Group (RTOG) criteria: nadir prostate-specific antigen (PSA) post radiotherapy concentration plus 2 ng/mL [13].

Written informed consent was obtained from all patients

Patients were clinically assessed during treatment on a weekly basis. Acute (during RT) and late ($\geqslant$90 days post treatment) GU and GI toxicities were documented based on Radiation Therapy Oncology Group (RTOG) Criteria for Adverse Events (www.RTOG.org). The maximum toxicity suffered was recorded.

Post treatment follow-up visits were performed by the treating radiation oncologist every 3 months for the first 2 years, followed by every 4–6 months for the next 3 years and yearly

Table 1 Baseline demographic and clinical characteristics of the whole group.

Characteristic	Number ($N = 29$)	%
Median age (range)		
64 years (50–81)		
⩽65 years	14	48
>65 years	12	53
Tumor stage		
T1	10	*34.5*
T2/T3*	19	*65.5*
Gleason score		
2–6	10	34.5
7	9	31
8–10	10	34.5
PSA		
⩽10 ng/mL	5	17
>10–⩽20 ng/mL	7	24
>20–⩽50 ng/mL	6	20
>50–⩽100 ng/dl	6	20
>100–⩽200 ng/dl	5	17
Risk group		
Low risk (LR)	5	17
Intermediate risk (IR)	4	14
High risk (HR)	20	69
ADT use		
Yes	24	82.8
Duration ⩽6 months	3	10.4
Duration >6 months	21	72.4
% of core involvement		
Median (range)	60 (20–100)	
*Baseline** sexual function*		
Full potency	–	–
Partial potency	8	27.5
Impotent	21	72.5

* One pt was T3.
** Pre-RT, ADT, androgen deprivation therapy; PSA, prostate-specific antigen.

thereafter. Successive PSA values were measured every 2–3 months. Toxicity occurring 90 days after the end of RT was classified as late toxicity.

Erectile function was assessed using a three-tier grading system at baseline (before RT) and after completion of Androgen Deprivation therapy (ADT) and at regular follow-up visits:

- *Full potency:* ability to have full erections adequate for penetration;
- *Partial potency:* ability to achieve penetration but either aids are needed or the patient reports difficulty in doing so; or
- *Impotent:* inability to achieve an erection adequate for penetration.

Simulation, contouring, and planning

Computed tomography (CT) was acquired in the supine position, with 2-mm thick slices from the upper abdomen to 5 cm below the ischial tuberosities after immobilization with Knee and feet support immobilization devices. Patients were instructed to have a comfortably full bladder and an empty rectum at CT acquisition and before each treatment.

Planning and dose parameters

All patients were treated using two arcs VMAT plan with 6–10 MV photons. The entire cohort was treated to a total dose of 70 Gy in 28 daily fractions (250 cGy/fraction) over 51/2–6 weeks.

The clinical target volume (CTV); CTV-70 was defined as the entire prostate and seminal vesicle (if involved); CTV-56 included the whole prostate and seminal vesicle (if not involved). CTV-50.4 included pelvic Lymph nodes (in high risk patients) or a 0.7-cm anisotropic expansion volume of the obturator, common, external and internal iliac vessels, with trimming from adjacent bone, muscle, bowel and bladder. The nodal CTV contouring started at the level of L5-S1; external iliac and obturator nodal volumes were drawn till the top of femoral head and symphysis pubis respectively. Pelvic lymph node volumes were drawn following the RTOG consensus recommendations.

The planning target volume (PTV)

PTV-70 was generated by adding anisotropic 0.5 cm margin to the CTV-70 apart from posteriorly where 0.3 cm margin was added (to decrease prostate-rectal interface dose) (Figs. 1 and 2). PTV-56 was a 0.7 cm anisotropic expansion from CTV56 except posteriorly (0.5–0.7 cm) depending on rectal fullness (Fig. 3). While for PTV-50.4; a margin of 0.3–0.5 cm was added to CTV 50.4 and 0.8–1.5 cm added volume anterior to S1–S3 (presacral nodes) (Fig. 4).

Contouring of the Organs at risk (OAR) followed the RTOG pelvic normal tissue contouring guidelines. The rectum was outlined from the level of the ischial tuberosities to the rectosigmoid flexure. The whole bladder was contoured; femoral heads were delineated to the level of the ischial tuberosities. The bowel was contoured as the entire volume of peritoneal space to within 1 cm of the cranial margin of the nodal PTV. Dose constraints used for the small bowel, rectum, bladder and PTV are shown in Table 2.

Online image-guided radiotherapy (IGRT)

Gold fiducial markers were implanted by the interventional radiologist under U/S guidance prior to radiotherapy for tracking purposes on daily imaging for verification and online correction. On Board imaging (OBI) Daily image guidance with Cone Beam CT (CBCT) was performed for all patients.

Statistical analysis

The collected data was analyzed using Kaplan–Meier method for biochemical relapse-free survivals (b-RFS) and comparisons were made using the log-rank test. Clinical characteristics were compared using the chi-square test or Fisher exact test for categorical variables. Statistical analysis was performed using SPSS ver. 20.0.0 software (SPSS Inc., Chicago, IL, USA).

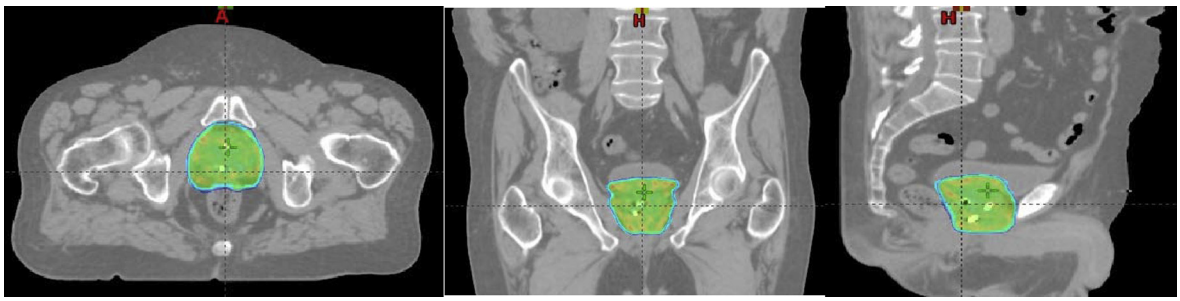

Figure 1 PTV70 (prostate only).

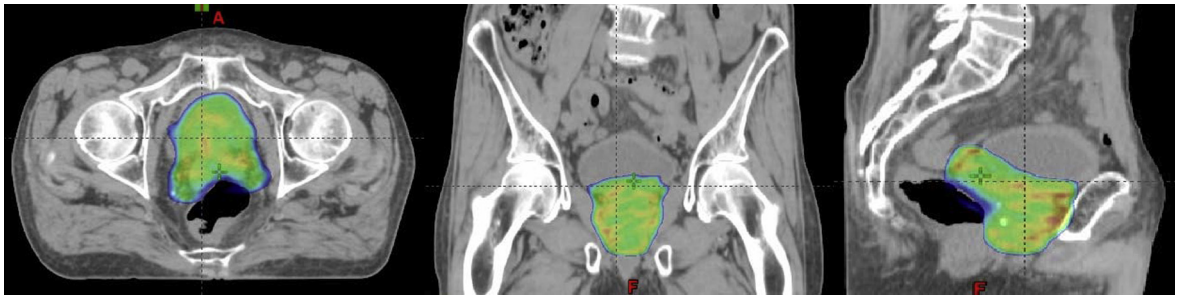

Figure 2 PTV70 (prostate + seminal vesicle if SV involved).

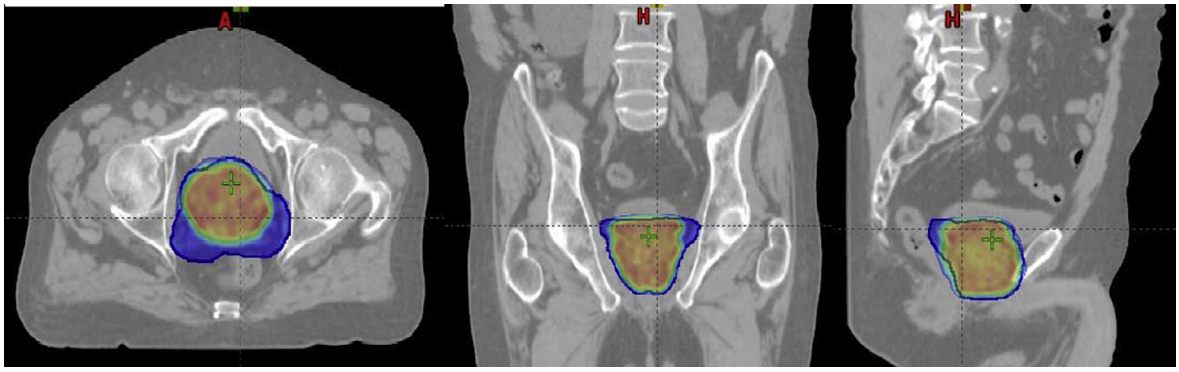

Figure 3 PTV56 (prostate + seminal vesicle).

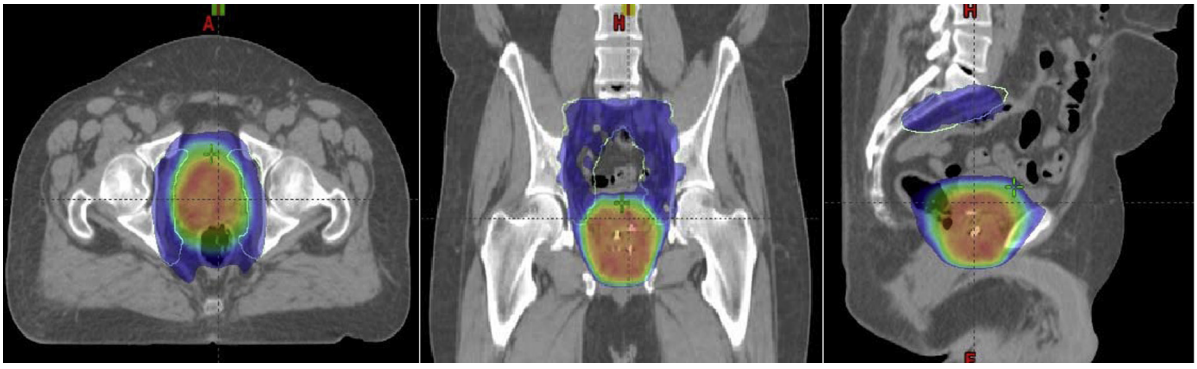

Figure 4 PTV50.4 (HR patients, lymph nodes included).

Table 2 Dose constraints of the studied LR/IM and HR prostate cancer patients.

PTV	⩾95% volume to receive 100% of prescribed dose
LR/IR	
Bladder	V60 < 25%
Rectum	V70 < 15%
Small bowel bag	mean dose < 35 Gy
HR	
Bladder	V50 < 50%
Rectum	< 10 cc volume to receive dose > 70 Gy
Small bowel bag	mean dose < 35 Gy

Results

The study included 29 patients; median age 64 years (50–81 years). T1–2 disease constituted 96.5%, initial PSA > 10 ng/ml was reported in 76%, GS ⩽ 7 was pathologically documented in 65% of the group. No ADT was reported for 5 patients (17%), those of the low risk (LR) group. Median time to post-treatment PSA nadir was 14 months (range: 7–32 months) with a mean/median of 3.2/0.5 ng/dl compared to pre-RT mean/median initial PSA of 50.5/38 ng/dl respectively (Table 1).

Erectile function and potency

Of the 29 patients, 8 had baseline (prior to RT) partial potency (27.5%) and the rest [21] were impotent (72.5%). Four out of the 8 patients (50%) retained functional potency on long-term follow-up (median 16 months; range: 14–32 months); all were among the low and Intermediate risk patients (Table 1).

Survival parameters

The 3 and 4 year actuarial overall survival for the whole group was 88% and 72% at a median FU of 42 months (range: 16–67 months) while the 2 and 3 years b-RFS for the whole group was 90% and 72% at a median FU of 34 months (range: 14–53 months). For age category of < 65 vs. ⩾65 years; the 4 actuarial overall survival was 71% and 74% and the actuarial 3 year b-RFS survival was 70% and 73% respectively.

Biochemical failure rates

The actuarial 3 year b-RFS for the whole group was 70%, with a median FU period of 34 months (range: 14–53 months). Only 4 patients of the high risk (HR) group with initial PSA > 100 ng/dl, developed biochemical failure at 9, 22, 25 and 26 months respectively; all of them developed bone metastases at 12, 27, 30 and 26 months, respectively. The calculated actuarial 3 year b-RFS rates for LR/IR and HR groups; based on the PSA-nadir plus 2 ng/mL; was 100%, and 48%, respectively ($p = 0.09$) Fig. 5 (a and b). Pretreatment PSA level ($p = 0.01$) and Gleason score ($p = 0.03$) were the only two significant factors for biochemical failure by univariate analysis (Fig. 5c and d). Percentage of positive biopsy cores ($p = 0.07$), and T-stage ($p = 0.09$) is shown in (Table 3). No prostate cancer-related deaths were observed in the group during the follow up period.

Treatment compliance

All patients tolerated the treatment well with no planned or unplanned treatment breaks. Radiotherapy treatment course was started after the 2nd month of Neo-adjuvant ADT and started with the 3rd ADT course. Overall treatment time was respected, no treatment breaks were encountered and all patients ended their RT course within the planned treatment duration (51/2–6 weeks [range: 39–44 days]).

GI toxicity

Acute GI toxicity scores were: grade 1 in 69% and grade 2 in 28% of patients. Late toxicity scores were: grade 0 in 80% and grade 1 in 20% of patients. There was no grade 3 or 4 acute or late GI toxicity with a median follow up of 42 months (Table 4).

GU toxicity

Acute GU toxicity scores were: grade 1 in 83% and grade 2 in 17% of patients. Late GU toxicity scores were: grade 0 in 50%, grade 1 in 40% and grade 2 in 10% of patients. There was no grade 3 or 4 acute or late GU toxicity with a median follow up period of 42 months (Table 4).

Discussion

This study highlights the first National (Kingdom of Saudi Arabia) experience in the Middle East Region using VMAT–SIB–ENI in the treatment of a selected group of 29 Prostate cancer patients treated with the hypofractionated schedule of 70 Gy delivered at 2.5 Gy/fraction using VMAT–SIB technique with pelvic lymph node treatment. The treatment results were encouraging and at least comparable to what has been achieved with other therapeutic approaches (IMRT–Brachytherapy) delivering high radiation doses in the treatment of prostate cancer in western patient's population series [14–16].

In the current study, Age, risk and percentage of hormone treatment (HT) among the studied subjects were comparable to others Table 1 [10,14–16]. Erectile/sexual function is usually affected in ~75% of the patients on long term ADT [17], about 1 in 5 men (20%) keep the ability to maintain an erection. In addition to obesity, comorbidities (Diabetes, CVDs) and pre-treatment sexual aid usage – all of which- increases patients' risk of radiation induced ED. In the current study only 8 patients (28%) reported baseline partial potency and 50% of them reported to be sexually active on long term follow up; a finding which is in agreement with the reported 43.6% baseline Sexual dysfunction (a score > 2 on the LENT/SOM scale) with a further score deterioration of 83.5% during neo-adjuvant hormone therapy and before radiotherapy; 26% of patients can expect to retain sexual function at 5 years after radiotherapy treatment. Partial recovery was reported after intermittent and continuous ADT in 16–28% and 10% respectively at a FU period of 15–24 months [17,18].

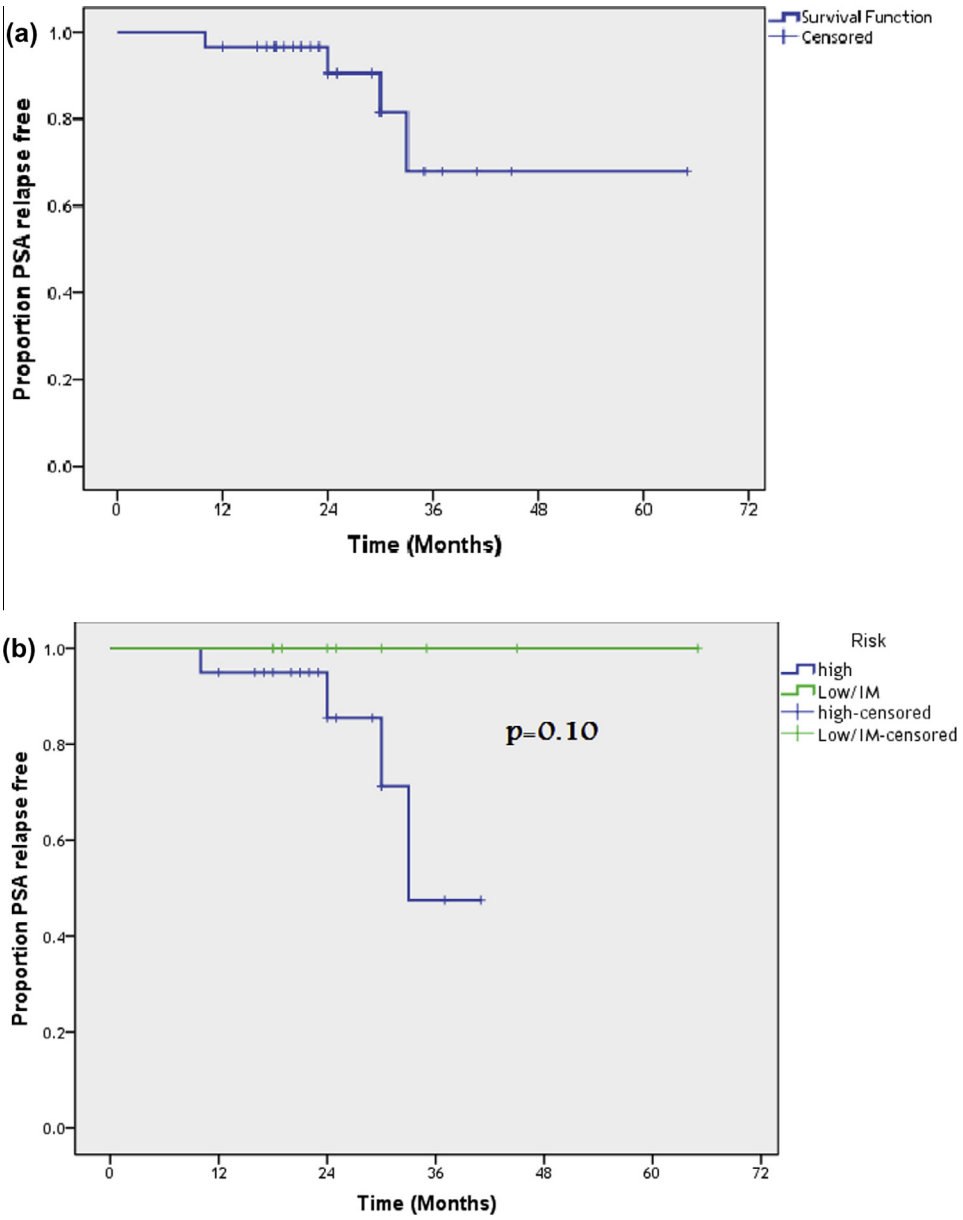

Figure 5 (a and b) Kaplan Meier estimates for PSA-bRFS for whole and LR/IR vs. HR groups treated by Hypo-Fx VMAT. (c) Kaplan Meier estimates for 29 patients. PSA-bRFS treated by Hypo-Fx VMAT (GS $\leqslant$ 7 vs. GS $>$ 7). (d) KM estimates for PSA-bRFS treated by Hypo-Fx VMAT (PSA $\leqslant$ 20 vs. PSA $>$ 20).

In the current study; the calculated 3-year b-RFS rates (PSA nadir plus 2 ng/mL) were 100%, and 47%, for low/intermediate and high risk patients respectively at a median follow up period of 34 months (range: 14–53 months). Results which are lower than a recently published Korean report using Hypo-fractionated IMRT for 30 patients. at a median FU period of 74.4 months (18.8–125.9) with 5-year actuarial b-RFS rates of 100%, and 88.5%, for low/intermediate, and high-risk patients respectively; in addition to that reported at the Cleveland Clinic Foundation for 770 patients. treated with the same hypo-fractionated IMRT schedule with a median FU of 66 months (8–86 months) with reported 5-year b-RFS of 94%, 83%, and 72%, for the low, intermediate and high risk patients' cohort respectively [19,20]. An explanation of which is that our cohort was recently treated after the introduction of the VMAT technology to the hospital in 2009 and hence longer follow up months are needed, in addition to the high initial PSA $>$ 100 ng/dl for all of the 4 relapsed patients.

High-risk group with high risk of metastases and Prostate Cancer Specific Mortality (PCSM) are those patients with a biopsy GS 8–10, high PSA $>$ 20–50 ng/dl and clinical stage cT3b–T4. Conversely, patients at low risk of metastases and PCSM are those with biopsy GS $<$ 7, clinical stage $<$cT3a and time to biochemical progression $>$ 3 years [21,22]. Similar finding in this study was reported with a better b-RFS for those patients with GS $\leqslant$ 7 and PSA $<$ 20 ng/dl compared to those with a higher score (Table 3).

Elective Pelvic node in addition to prostate irradiation aiming at dose escalation using IMRT might lead to a better treatment outcome in HR prostate cancer patients, with

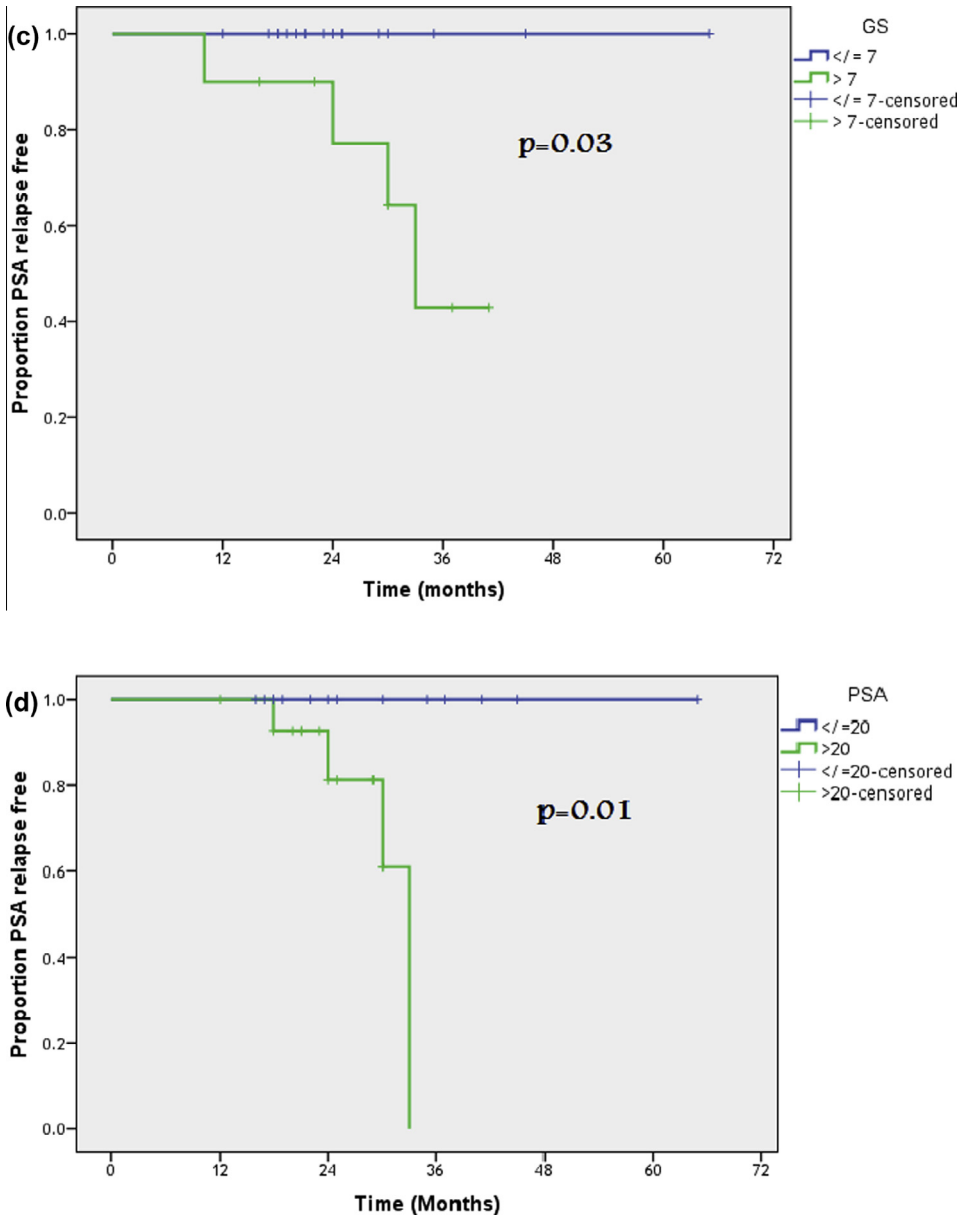

Fig. 5 (*continued*)

acceptably low acute and late bowel toxicity. Acute RTOG grade $\geqslant 2$ bowel toxicity was 40% and 50% for 50 and 55 Gy respectively, suggesting both volume and dose relationships for acute effects. While, late RTOG diarrhea grade $\geqslant 2$ was reported with a larger bowel volume (BV) irradiated (BV40 > 124 cm^3 ($p = 0.04$), BV45 > 71 cm^3 ($p = 0.03$) and BV60 > 2 cm^3 ($p = 0.01$) [23].

Acute and late GI/GU toxicities of the current study compared to other series (Tables 4 and 5); showed a slightly higher acute GI grade $\geqslant 2$ toxicity compared to other studies [18,24–27] albeit a lower % of late GI grade $\geqslant 2$ toxicity and comparable acute/late GU toxicities, a finding which might be explained by the larger BV irradiated during pelvic ENI.

Hypo-fractionated VMAT radiotherapy was not inferior to standard fractionated radiotherapy in terms of acute genitourinary and gastrointestinal toxicity for patients with intermediate and high-risk prostate cancer.

Two important issues addressing prostate cancer RT need to be discussed:

First issue: Hypo-fractionation and its equivalence to standard fractionation schedules; According to the presumed α/β ratio for prostate cancer using the linear quadratic model, the BED of 70 Gy delivered at 2.5 Gy/fraction would be about 85 Gy (α/β: 1.5) and about 74 Gy (α/β:10) if delivered at 1.8 Gy/fraction [28].

Accurate α/β ratio is still controversial; a meta-analysis of 25 studies with > 14,000 patients concluded an α/β ratio of approximately 1.5 Gy due to its slow growth. Based on this assumption, hypofractionated radiotherapy (HFRT)

Table 3 Potential prognostic factors for PSA biochemical relapse-free survival (b-RFS).

Factors	No. of patients.	PSA-relapse free survival %			
		1 years	2 years	3 years	*p* value
All	29	97	90	70	NA
Age (median 64 years)					
<65	15	100	87	70	0.325
$\geqslant 65$	14	100	92	73	
T-stage					
T1	10	100	100	100	0.09
T2–T3	19	94	84	47	
Gleason score					
$\leqslant 7$	19	100	100	100	
>7	10	90	75	43	**0.02**
PSA					
<20	12	100	100	100	**0.01**
$\geqslant 20$	17	92	81	61	
Risk group					
LR/IR	9	100	100	100	0.09
HR	20	100	85	48	

LR, low risk; IR, intermediate risk; HR, high risk.

Table 4 GI/GU toxicity results in relation to the study risk groups.

	Acute grade 2 toxicity		Late grade 2 toxicity	
	GI No. (%)	GU No. (%)	GI No. (%)	GU No. (%)
LR/IR	3 (11%)	2 (6.7%)	0%	1 (3.4%)
HR	5 (17%)	3 (10%)	0%	2 (6.8%)
p-value	0.45	0.28	–	0.24

LR: low risk, IR: intermediate risk, HR: high risk.

could be more effective than conventional fractionation with fraction sizes of 1.8–2 Gy, in addition to being more convenient for the patient with lower costs for the health care system [29].

Table 6 summarizes the ongoing phase-III randomized controlled trials (RCTs) for low/intermediate risk prostate cancer patients trying to answer whether HFRT is equivalent to conventionally fractionated radiotherapy (CFRT) in terms of b-RFS and toxicity. RTOG 0415- phase III (RCT) and a phase I/II trial by Kupelian et al. [18] demonstrated an equivalence between both fractionation regimens. If the $\alpha/\beta = 10$ but with an $\alpha/\beta = 1.5$, HFRT should produce better rates of biochemical control because being less than the reported $\alpha/\beta = 3$ Gy for late reactions of neighboring OARs (including rectum). An assumption which was proved by the CHHip [22] trial showing that HFRT was equally well tolerated compared to CFRT treatment at 2 years with suggested α/β values as low as 1.5 Gy.

The second issue: Radiation delivery technique and toxicities

Radiation therapy GI and GU toxicities reported from previous hypo-fractionation schedules were due to the use of conventional non-conformal RT techniques but with modern conformal tailored, sophisticated treatment plans with improved targeting and treatment delivery techniques (e.g.: IMRT–VMAT) with the implementation of image guidance using daily cone beam CT (CBCT) a better tolerated treatment outcome with possible improvement in the PSA control is expected [30].

Intra-fraction motion (real-time motion of the prostate during treatment delivery) is only lately being characterized. Until the target (i.e., the prostate) position is accurately hit every day during actual radiation delivery, the benefits of hypofractionation with EBRT will be questioned. Although localization and motion problems are important, independent of any fractionation schedule, the margin of error for a smaller number of fractions could be smaller compared with a larger number of fractions. This is

Table 5 GI/GU study toxicity results compared to other series.

Trial	Dose#Fx	Acute $\geqslant$ G2 toxicity		Late $\geqslant$ G2 toxicity	
		GI No. (%)	GU No. (%)	GI No. (%)	GU No. (%)
CHHiP[24]	74 Gy#37	3 (2.3%)	9 (7%)	6 (4.3%)	3 (2.2%)
	60 Gy#20	3 (2.3%)	10 (7.6%)	5 (3.6%)	3 (2.2%)
	57 Gy#19	1 (0.8%)	9 (7%)	2 (1.4%)	0%
HYPRO[25]	78 Gy#39	42 (13%)	73 (22%)	–	–
	64.6 Gy#19	43 (13%)	75 (23%)	–	–
ISHII[26]	VMAT			–	–
	78 Gy#39	18 (18%)	13 (13%)		
Kupelian[20]	70 Gy#28	23 (23%)	19 (19%)	10 (10%)	13 (12%)
Lips[27]	76 Gy#35	98 (30%)	160 (47%)	72 (22%)	42 (13%)
Current study*	70 Gy#28	***8 (28%)***	***5 (17%)***	***0%***	***3 (10%)***

* No grade 3/4 toxicity was recorded.

Table 6 Ongoing phase III studies comparing conventional and hypo-fractionated-RT.

Trial	Identifier	Status	Estimated No.	Total dose (Gy)	Risk
RTOG 0415	***NCT00331773***	Unknown	1067	*70#28*	Low
UK MRC/CHHiP	***NCT00392535***	Accruing	3216	74#37	Low
				57#19 & 60#20	Intermediate
NCIC	***NCT00304759***	Ongoing	1204	78#39 & *60#20*	Intermediate
MD Anderson	***NCT00667888***	Ongoing	225	78#39 &*60#20*	Low Intermediate

currently untested and should be the subject of future investigations.

Conclusion

This is the first published report in the Middle East evaluating feasibility, treatment related toxicities of high dose hypo-fractionation VMAT–SIB–ENI–RT for HR prostate cancer patients with acceptable PSA b-RFS. Acute and late GU and GI toxicities are comparable to international reports. Hypo-fractionated VMAT–SIB–ENI is safe and a feasible dose escalation method; a novel technique in RT treatment delivery that needs further assessment in prospective randomized controlled trials.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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